Amendments to the Claims

Claim 1 has been amended without any intention of disclaiming equivalents thereof. Claims 11, 15, and 26-30 have been cancelled without prejudice to their subsequent reintroduction into this application or their introduction into a related application. The following list of claims replaces all prior versions and lists of claims in the application.

Listing of Claims:

1. (Currently amended) A method for detecting the presence ~~and location~~ or absence of a post-translational modification at a location on a target protein within a sample, comprising:

(1) computationally analyzing an amino acid sequence of said target protein to identify one or more potential sites for said post-translational modification;

(2) computationally identifying an amino acid sequence of at least one fragment of said target protein, said fragment predictably resulting from a treatment of said target protein within said sample, and said fragment comprising at least one of said potential post-translational modification sites and, separate therefrom, a PET (proteome epitope tag) unique to said fragment within said sample;

(3) generating a capture agent that specifically binds said PET separate from said post-translational modification on said fragment, and immobilizing said capture agent to a support;

(4) subjecting said sample to ~~a~~ the treatment to ~~render~~ produce said fragment, rendering said fragment soluble in solution, and contacting said ~~sample after said treatment~~ fragment with said capture agent to bind said fragment, at said PET, to said capture agent;

(5) detecting, on said fragment bound to said capture agent, the presence or absence of said post-translational modification by using a secondary capture agent specific for said post-translational modification separate from said PET on said fragment, wherein said secondary capture agent is labeled by a detectable moiety.

2. (Original) The method of claim 1, wherein said post-translational modification is acetylation, amidation, deamidation, prenylation, formylation, glycosylation, hydroxylation, methylation,

myristoylation, phosphorylation, ubiquitination, ribosylation or sulphation.

3. (Original) The method of claim 2, wherein said post-translational modification is phosphorylation on tyrosine, serine or threonine.

4. (Previously Presented) The method of claim 1, wherein said step of computationally identifying an amino acid sequence includes a Nearest-Neighbor amino acid Analysis that identifies said PET based on criteria that also include one or more of pI, charge, steric, solubility, hydrophobicity, polarity and solvent exposed area.

5. (Original) The method of claim 4, further comprising determining the specificity of said capture agent generated in (3) against one or more nearest neighbor(s), if any, of said PET.

6. (Original) The method of claim 5, wherein peptide competition assay is used in determining the specificity of said capture agent generated in (3) against said nearest neighbor(s) of said PET.

7. (Previously Presented) The method of claim 1, wherein said step of computationally identifying an amino acid sequence includes a solubility analysis that identifies a said PET that is predicted to have at least a threshold solubility under a designated solution condition.

8. (Previously Presented) The method of claim 1, wherein the length of said amino acid sequence of at least one fragment of said target protein is selected from 15-20 amino acids, 20-25 amino acids, 25-30 amino acids, or 30-40 amino acids.

9. (Original) The method of claim 1, wherein said capture agent is a full-length antibody, or a functional antibody fragment selected from: an Fab fragment, an $F(ab')_2$ fragment, an Fd fragment, an Fv fragment, a dAb fragment, an isolated complementarity determining region (CDR), a single chain antibody (scFv), or derivative thereof.

10. (Previously Presented) The method of claim 1, wherein said capture agent is selected from nucleotides; nucleic acids; PNA (peptide nucleic acids); proteins; peptides; carbohydrates; artificial polymers; or small organic molecules.

11. (Cancelled)

12. (Original) The method of claim 1, wherein said treatment is denaturation and/or fragmentation of said sample by a protease, a chemical agent, physical shearing, or sonication.

13. (Original) The method of claim 12, wherein said denaturation is thermo-denaturation or chemical denaturation.

14. (Original) The method of claim 13, wherein said thermo-denaturation is followed by or concurrent with proteolysis using thermo-stable proteases.

15. (Cancelled)

16. (Original) The method of claim 12, wherein said fragmentation is carried out by a protease selected from trypsin, chymotrypsin, pepsin, papain, carboxypeptidase, calpain, subtilisin, gluc-C, endo lys-C, or proteinase K.

17. (Original) The method of claim 1, wherein said sample is a body fluid selected from: saliva, mucous, sweat, whole blood, serum, urine, amniotic fluid, genital fluid, fecal material, marrow, plasma, spinal fluid, pericardial fluid, gastric fluid, abdominal fluid, peritoneal fluid, pleural fluid, synovial fluid, cyst fluid, cerebrospinal fluid, lung lavage fluid, lymphatic fluid, tears, prostatitc fluid, extraction from other body parts, or secretion from other glands; or from supernatant, whole cell lysate, or cell fraction obtained by lysis and fractionation of cellular material, extract or fraction of cells obtained directly from a biological entity or cells grown in an artificial environment.

18. (Previously presented) The method of claim 1, wherein said sample is obtained from human, mouse, rat, frog, fish, fly, nematode, fission or budding yeast, or plant.

19. (Previously presented) The method of claim 1, wherein said sample comprises membrane bound proteins.

20. (Original) The method of claim 1, wherein said treatment is carried out under conditions to preserve said post-translational modification.

21. (Cancelled)

22. (Original) The method of claim 1, wherein said capture agent is optimized for selectivity for said PET under denaturing conditions.

23. (Previously presented) The method of claim 1, wherein said secondary capture agent is labeled by a detectable moiety selected from: an enzyme, a fluorescent label, a stainable dye, a chemilumninescent compound, a colloidal particle, a radioactive isotope, a near-infrared dye, a DNA dendrimer, a water-soluble quantum dot, a latex bead, a selenium particle, or a europium nanoparticle.

24. (Original) The method of claim 23, wherein said post-translational modification is phosphorylation, and said secondary capture agent is a labeled secondary antibody specific for phosphorylated tyrosine, phosphorylated serine, or phosphorylated threonine.

25. (Original) The method of claim 24, wherein said secondary antibody is labeled by an enzyme or a fluorescent group.

26-30. (Cancelled)

31. (Original) The method of claim 1, wherein said sample contains billion molar excess of unrelated proteins or fragments thereof relative to said fragment.

32. (Previously presented) The method of claim 1, further comprising quantitating the amount of said fragment bound to said capture agent.

33. (Previously Presented) The method of claim 1, wherein step (3) is conducted by immunizing an animal with an antigen comprising said PET sequence.

34. (Original) The method of claim 33, wherein the N- or C-terminus, or both, of said PET sequence are blocked to eliminate free N- or C-terminus, or both.

35. (Original) The method of claim 34, wherein the N- or C-terminus of said PET sequence are blocked by fusing the PET sequence to a heterologous carrier polypeptide, or blocked by a small chemical group.

36.- 125. (Cancelled).

126. (Previously Presented) The method of claim 3, wherein said post-translational modification is phosphorylation on tyrosine.

127. (Previously presented) The method of claim 24, wherein said post-translational modification is phosphorylation, and said secondary capture agent is a labeled secondary antibody specific for phosphorylated tyrosine.

128. (Cancelled)

129. (Previously presented) The method of claim 9, wherein said capture agent is a full-length antibody.

130. (Previously presented) The method of claim 23, wherein said secondary capture agent is labeled by a fluorescent label.

131. (Previously presented) The method of claim 25, wherein said secondary antibody is labeled by a fluorescent group.

132. (Previously presented) The method of claim 127, wherein said secondary antibody is labeled by a fluorescent group.